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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/895,517	06/28/2001	Ralf Wolleschensky	GK-ZEI-3099/500343.20099	8222

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EXAMINER

PRITCHETT, JOSHUA L

ART UNIT

PAPER NUMBER

2872

DATE MAILED: 09/30/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.

09/895,517

Applicant(s)

WOLLESCHENSKY ET AL.

Examiner

Joshua L Pritchett

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-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

- 1) ☐ Responsive to communication(s) filed on _____.
- 2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

- 4) ☒ Claim(s) 1-86 is/are pending in the application.
- 4a) Of the above claim(s) _____ is/are withdrawn from consideration.
- 5) ☐ Claim(s) _____ is/are allowed.
- 6) ☒ Claim(s) 1-86 is/are rejected.
- 7) ☐ Claim(s) _____ is/are objected to.
- 8) ☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☒ The drawing(s) filed on 28 June 2001 is/are: a) ☒ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- 11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.
- If approved, corrected drawings are required in reply to this Office action.
- 12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

- 13) ☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☒ All b) ☐ Some * c) ☐ None of:
1. ☒ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).
- * See the attached detailed Office action for a list of the certified copies not received.
- 14) ☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).
- a) ☐ The translation of the foreign language provisional application has been received.
- 15) ☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

- 1) ☒ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
- 3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) 5.
- 4) ☐ Interview Summary (PTO-413) Paper No(s). _____.
- 5) ☐ Notice of Informal Patent Application (PTO-152)
- 6) ☐ Other: _____.

DETAILED ACTION

Information Disclosure Statement

The information disclosure statement filed March 29th 2002 fails to comply with 37 CFR 1.98(a)(2), which requires a legible copy of each U.S. and foreign patent; each publication or that portion which caused it to be listed; and all other information or that portion which caused it to be listed. No copy of the crossed off documents was found in the information disclosure statement and therefore the crossed off documents were not considered. All other documents were considered.

Claim Objections

Claims 4, 6, 7, 8 and 10-17 fail to recite the additional steps in active form. Please eliminate the passive voice from the claims to make the claimed subject matter more concise.

Applicant is advised that should claim 36, 38 or 42 be found allowable, claims 40, 47 or 45 respectively will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

Claims 1-57 objected to based on the lack of antecedent basis in the following instances.

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Claims 7 and 52 recite the limitations "the weighted channels" and "the detection channels" in lines 2-3. There is insufficient antecedent basis for this limitation in the claim.

Claims 8 and 53 recite the limitation "the signals" and "the weighted signals" in lines 1 and 4 respectively. There is insufficient antecedent basis for this limitation in the claim.

Claims 10 and 55 recite the limitation "the weighting and summing" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claims 12 and 57 recite the limitation "the resistances" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 14, 27, 28, 69, and 70 recite the limitation "the signals" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claim 16 recite the limitation "the characteristic response curve" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 17, 19, 22, 59, 61 and 64 recite the limitation "the position signal" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 18 and 60 recite the limitation "the individual channels" in line 2. There is insufficient antecedent basis for this limitation in the claim.

Claims 24 and 66 recite the limitation "the operating mode" and "the detection channel" in line 4. There is insufficient antecedent basis for this limitation in the claim.

Claims 25 and 67 recite the limitation "the respective detection channels" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 26 and 68 recite the limitation "the relevant spectral region" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 29 and 71 recite the limitation "the photon counting" in line 1. There is insufficient antecedent basis for this limitation in the claim.

Claims 37 and 79 recite the limitation "the illumination means" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim.

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1, 2, 3, 24, 25, 48 and 66 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention. The term "and/or" does not enable the examiner to readily determine the metes and bounds of the claim, because the term does not limit the clearly delineate the claimed subject matter. The examiner cannot determine whether the applicant intends to claim a centroid measurement or a maximum measurement. Claims 2-47 and 49-86 are also objected to as being dependent on rejected claims based on the 35 U.S.C. 112 rejections of claims 1 and 48.

Claim Rejections - 35 USC § 102

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The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 1-3, 7, 10, 14, 20, 21, 24, 25, 26, 32, 42, 43, 45, 48, 52, 55, 62, 63, 66, 67, 68, 74, 83, and 84 rejected under 35 U.S.C. 102(b) as being anticipated by Yang (US 5,859,700).

Regarding claims 1 and 48, Yang discloses a method for optical detection of characteristic quantities of the wavelength-dependent behavior of an illuminated specimen, such as the emission behavior and/or absorption behavior, preferably the fluorescence and/or luminescence and/or phosphorescence and/or enzyme-active light emission and/or enzyme-active fluorescence (col. 2 lines 31-32). Yang further teaches absorption behavior determining at least one spectral centroid and/or maximum of emission radiation and/or absorbed radiation (col. 3 line 32). In this case peak is taken to mean the same as a maximum.

Regarding claims 2 and 3, Yang teaches the determination of the centroid and/or of the maximum of the emission radiation of fluorochromes is carried out for distinguishing different dyes and/or determine the local dye composition of an image point when a plurality of dyes are used simultaneously and/or determine the local shift of the emission spectrum depending on the local environment to which the dye or dyes is or are attached and/or for measuring emission ratio dyes for determining ion concentration (col. 3 lines 32-35).

Regarding claims 7 and 52, Yang further teaches spectral weighting carried out between a plurality of detection channels, summing of the weighted channels of the signals of the detection and summing the detection channels (col. 5 lines 55-56).

Regarding claims 10 and 55, Yang teaches signal detection conversion to digital and reading out of the converted signal and the weighting and summing carried out digitally in a computer (col. 6 lines 15-23, col. 17 lines 26-28).

Regarding claim 14, Yang further teaches the signals of the detector channels are influenced by nonlinear distortion of the input signals (col. 26 line 1). In this case experimental noise is taken to mean the same thing as nonlinear distortion.

Regarding claims 20 and 62, Yang further teaches the use of color-coded fluorescence imaging (col. 6 lines 27-29).

Regarding claims 21 and 63, Yang further teaches the superposition of additional images (col. 6 lines 27-29). In this case the superposition of different images is taken to mean the changing of the image over the course of time or the overlap of different pixel groups in the image.

Regarding claims 24 and 66, Yang further teaches a comparison of the measured signal to a reference carried out by comparators in detection channels and in case the reference signal is not reached and/or is exceeded a change in the operating mode of the detection channel occurs (col. 25 line 31- col. 26 line 17).

Regarding claims 25 and 67, Yang further teaches that respective detection channel is switched off and/or not taken into account if the reference signal is not reaches and/or is exceeded (col. 26 lines 9-11).

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Regarding claims 26 and 68, Yang further teaches the relevant spectral region is narrowed (col. 25 lines 7-8).

Regarding claims 32 and 74, Yang further teaches the use of the spectral detection in a microscope (col. 25 line 7).

Regarding claims 42, 45 and 83, Yang further teaches the use of brightfield imaging (col. 6 lines 5-6).

Regarding claims 43 and 84, Yang further teaches the use of point imaging (col. 3 line 39).

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 4-6, 8, 9, 13, 15, 17-19, 49-51, 53, 54 and 58-61 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Okubo (EP 463 600).

Regarding claims 4-6 and 49-51, Yang teaches the invention as claimed, but lacks reference to the splitting of the emission radiation by a dispersive element. Okubo teaches the use of a dispersive element to split the emission radiation for the sample being examined (page 10 lines 31-33). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use a dispersive element to split the emission radiation entering the Yang

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invention for the purpose of sending the signal to several different detectors for data processing and analysis.

Regarding claims 8, 9, 13, 53, 54, and 58, Yang further lacks the use of a weighting curve in the analysis of the data collected. Okubo teaches the use of both straight line and adjustable weighting curve during data analysis (page 7 lines 19-34). In this case the equations provided by Okubo are taken to be numerical representations of the equations that determine the weighting curve. It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use a weighting curve to analyze the data collected by the Yang invention for the purpose of quicker and more precise calculations through the use of a reference material.

Regarding claim 15 and 16, Yang further lacks the influence of experimental noise on integration parameters and amplification during the data analysis process. Okubo teaches that the integration parameters and amplification are adjustable based on the signal input (page 7 lines 19-34). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to make the integration parameters and the amplification of the signal adjustable for the purpose of collecting more precise results from the experimentation through the elimination of experimental noise.

Regarding claims 17 and 59, Yang does teach the conversion of the signal from analog to digital (col. 25 lines 35-36).

Regarding claims 18 and 60, Yang further lacks the weighting of the signals from the individual channels through the use of weight curves. Okubo teaches the use of weight curves and the application of weight curves in summing the results from different channels (page 7 lines 19-34). It would have been obvious to a person of ordinary skill in the art at the time the

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invention was made to use a weighting curve to analyze the data collected by the Yang invention for the purpose of more precise and reliable calculations.

Regarding claims 19 and 61, Yang also teaches the sum signal generating an image (col. 25 lines 29-30).

Claims 11, 12, 27, 56, 57, and 69 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Lee (US 5,737,077).

Regarding claims 11 and 56 Yang teaches the invention as claimed but lacks the dimension of analog processing through the use of resistance cascade. Lee teaches the use of resistors in combination as a means of processing the collected data (col. 10 lines 28-34). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use resistors in combination as a data processing means within the Yang invention for the purpose of sorting the intensity of the light emission by the amount of electricity created by the photons contacting the detector.

Regarding claims 12 and 57 Yang further lacks adjustable resistance within the resistors used to process the data collected. Lee teaches the use of adjustable resistors (col. 10 line 34). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use adjustable resistors for the purpose of increased flexibility in the application of the Yang invention.

Regarding claims 27 and 69 Yang further lacks signals of detection channels being generated by an integrator circuit. Lee teaches the use of an integration circuit to generate the signal of a detection channel (col. 10 lines 28-34). It would have been obvious to a person of

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ordinary skill in the art at the time the invention was made to use an integrator circuit in the generation of the signals from the Yang invention for the purpose of quick and reliable conversion of the light intensity to an electronic signal usable by a computer.

Claims 22, 23, 64 and 65 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Okubo as applied to claims 8 and 53 above, and further in view of Hochman (US 6,319,682).

Yang in view of Okubo teaches the invention as claimed but lacks the use of either a weighting curve or a lookup table. Hochman teaches the use of a lookup table for use in combination with position and sum signals as well as in the representation of different dyes and/or the spread of the generated image (col. 12 lines 12-15). It would have been obvious to a person of ordinary art at the time the invention was made to use a lookup table as described in Hochman in combination with the Yang in view of Okubo invention for the purpose of making the generated images easier to understand and to increase the speed of data analysis.

Claims 28-30, 34, 70-72, and 76 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Kash (US 6,342,701).

Regarding claims 28 and 70 Yang teaches the invention as claimed but lacks a specific reference to photon counting. Kash teaches the use of photon counting as a means to determine the intensity of light emitted from a sample (col. 7 lines 46-48). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use a photon detector as a

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means of collecting the emission intensity for the Yang invention because the use of a photon detector is commonly known in the art.

Regarding claims 29 and 71 Yang further lacks photon counting carried out in a time relation. Yang does teach a time dependent relationship within the invention (col. 5 lines 36-37). Kash teaches the use of time related photon counting (col. 3 lines 5-20). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use time related photon counting in the Yang invention for the purpose of measuring how the emissions of the sample change with respect to time.

Regarding claims 30, 34, 72, and 76, Yang further lacks the specific mention of the detection of single photons or multiphoton fluorescence. Kash teaches the detection of multiphoton fluorescence (col. 6 lines 47-48). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use single or multiphoton fluorescence detection within the Yang invention for the purpose of collecting data related to the intensity of the emission of the sample being examined.

Claims 35, 39, 41, 44, 46, 77, 81, 82, 85, and 86 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Simon (US 6,356,088).

Regarding claims 25, 39, 46, 77, 81 and 86, Yang teaches the invention as claimed but lacks reference to either confocal or nonconfocal detection. Simon teaches the use of both confocal and nonconfocal detection (col. 4 line 2). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use either confocal or nonconfocal

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detection in combination with the Yang invention for the purpose of focusing the emission of the sample to the appropriate location of a detector.

Regarding claims 41, 44, 82 and 85, Yang further lacks reference to either descanning or nondescanning detection. Simon teaches the use of either descanning or nondescanning detection (col. 3 lines 12-13). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use either descanning or nondescanning detection within the Yang invention for the purpose of determining the emission of the sample being tested.

Claims 33, 36, 37, 38, 40, 47, 75, 78, 79 and 80 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Yagi (US 5,986,256).

Regarding claims 33 and 75, Yang teaches the invention as claimed but lacks reference as to the method of scanning the sample during data collection. Yagi teaches a scanning microscope (col. 2 lines 6-7). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to use a scanning microscope within the Yang invention for the purpose of collecting data from a wide spatial range within the test sample and to allow the ability to pinpoint a specific location within the sample.

Regarding claims 36, 40 and 78, Yang further lacks a scanning arrangement for the microscope. Yagi teaches a scanning arrangement (col. 4 lines 3-4). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to provide the Yang invention with a scanning arrangement for the purpose of collecting data from a wide spatial range within the test sample and to allow the ability to pinpoint a specific location within the sample.

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Regarding claims 37, 38, 47, 79, and 80, Yang further lacks reference to either an X-Y scanning table or illumination means for a scanning means. Yagi teaches the use of an X-Y scan table (col. 4 lines 3-4). Yagi further teaches a means of illumination for the X-Y scanning means (col. 4 lines 1-2). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to provide the Yang invention with an X-Y scanning table and a means of illumination for the X-Y scanning means for the purpose of collecting data from a wide spatial range within the test sample and to allow the ability to pinpoint a specific location within the sample.

Claims 31 and 73 are rejected under 35 U.S.C. 103(a) as being unpatentable over Yang in view of Tuunanen (US 6,084,680).

Yang teaches the invention as claimed, but lacks reference to the placement of the sample on a microtiter plate. Tuunanen teaches the placement of a samples used in fluorescence microscopy on a microtiter plate (col. 2 lines 45-47). It would have been obvious to a person of ordinary skill in the art at the time the invention was made to place the sample on a microtiter plate because this practice is widely known and used in the art.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Joshua L Pritchett whose telephone number is 703-305-7919. The examiner can normally be reached on Monday - Friday 7:00 - 3:30.

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If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Cassandra Spyrou can be reached on 703-308-1687. The fax phone numbers for the organization where this application or proceeding is assigned are 703-308-7722 for regular communications and 703-308-7724 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is 703-308-0956.

JLP

September 19, 2002

A handwritten signature in black ink, appearing to be 'C. Spyrou', with a long horizontal flourish extending to the right.

Cassandra Spyrou
Supervisory Patent Examiner
Technology Center 2800